

Remarks

By the instant Amendment, Claims 90-123 have been added to more broadly cover the subject matter of the invention. Withdrawal of the rejections and allowance of the claims are respectfully requested.

Pursuant to 37 C.F.R. §1.121(c)(1)(ii), since claims 10-13 have been added, no marked up versions of these added claims have been supplied.

I. Withdrawal of Claims 69-87

Claims 69-87 were withdrawn as being directed to a non-elected invention. Applicants respectfully traverse this withdrawal of claims 69-87 because examination of these claims would not require any additional work (e.g. additional searching) or expense. See MPEP 818. Specifically, the apparatus recited in claims 69-87 mirror the method claims recited in claims 88-107. Reconsideration and withdrawal of the election requirement are respectfully requested.

II Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 88 and 89 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner continues to dispute the terms "thermal bridge" and "biopharmaceutical products" despite numerous explanations, references to support in the Specification and Declarations from those skilled in the art.

Applicants respectfully and most strenuously traverse this rejection and reiterate the arguments set forth in the Amendment and Response filed January 7, 2002 and Supplemental Response on January 24, 2002.

Regarding the term "thermal bridge," Applicants respectfully submit that the Specification enables persons of ordinary skill in the art to determine how the heat exchange structure must be positioned within the interior cavity in order to form a thermal bridge by the medium between one or more of the heat transfer members and the interior wall. Specifically, the Specification provides at page 6, lines 8-14 the following:

In general, the system should be constructed such that the distance to be bridged by the thermal transport bridge will be a function of the thermal properties of the medium and the system, manufacturing requirements and construction processes used to build the system, and other relevant parameters of the system and components used. The size of the gap to be filled by the bridge can be determined through simple trial and error:

The Specification further provides, on page 6, lines 23-27, clear examples of how close the heat exchange members may be. Specifically, the Specification states that in one aspect of the present invention, the optimum gap is less than 2 inches, preferably less than 1 inch, even more preferably less than 1/4 inch, and most preferably less than 1/8 inch. Therefore, Applicants respectfully submit that the Specification enables one skilled in the art to practice the invention without undue experimentation.

Further, claim 88 specifically recites that a thermal bridge is formed in a gap between the heat transfer member and the interior wall in response to the interior wall being

actively cooled. Despite the Examiner comments in the Office Action to the contrary, Applicants respectfully submit that claim 88 is not directed to a thermal bridge formed during heating or thawing.

Applicants also respectfully submit that the definition of "biopharmaceutical product" supported by the Declarations of Burman, Lawlis, Jr. and Vetterlein is not in conflict with the one offered in the specification. Simply stated, if, for example, a particular type of the products listed in the Specification does not derive from a biological source or is not regulated by the FDA, then it would not be considered a biopharmaceutical product under the definition. The Examiner has failed to provide any proof that the FDA regulates water or orange juice as a biopharmaceutical product, but continues to rely on this position in rejecting this term. Certainly, people of ordinary skill in the art can apply this definition to determine whether or not a particular product is or isn't a biopharmaceutical product as recited in the claims.

III. Applicants Are Not In Possession Of Information About or the Actual 1992 Genentech Container

As clearly stated in the Declaration of Richard Wisniewski, Exhibits B, C and D of the Declaration reasonably resemble the temperature distributions of the 1992 Genentech container to the best of Mr. Wisniewski's knowledge. These temperature profiles were created at the request of the Examiner for his understanding during a previous telephonic interview. As the Examiner undoubtedly knows, there is absolutely no teaching or suggestion in the 1992 Wisniewski and Wu publication that a thermal bridge is formed by the arrangement of the fins in the 1992 Genentech container.

Instead, the Examiner relies upon his knowledge from his masters degree in Engineering from Princeton University to reject the temperature profiles offered by Mr. Wisniewski, who has over 26 years of experience in applied research, process and product development, process control, equipment and device design, industrial facility design and project and team management in the biopharmaceutical field. Applicants respectfully traverse the Examiner's assertions and also the Examiner's reliance on scientific theory (e.g. Fourier's law of heat conduction on page 4 of the Office Action) in support of his rejections and request that evidentiary support of the existence and meaning of the assertions and theories as they apply to the present invention be provided and produced by the Examiner.

Contrary to the Examiner's indication in the Official Action, Applicants are not in possession of the 1992 Genentech container or additional material information relating to the container (e.g. diameter, volume of container, dimension of the fins, how close to the wall of the container the heat transfer fins extended) not already disclosed in the 1992 disclosure of Wisniewski and Wu. Applicants do not work for Genentech, which, presumably, has exclusive control of the containers and information related to the containers, if such container or information still exists. Therefore, Applicants have no way in which, and are not required, to obtain actual measured results or computer generated results of the 1992 Genentech container.

Since Applicants are not in possession of this information and have no rights to access such information, there is no requirement under Rule 1.56 or Rule 1.105. Applicants respectfully submit that they have disclosed as much information regarding the 1992 Genentech container that is known to them in

the form of the 1992 publication. No other information concerning this 1992 Genentech container is in their possession.

Moreover, Applicants respectfully submit that they fully disclosed all known prior art relevant to the claimed invention.

The clear fact remains, however, that the Examiner has failed to point out any reference that disclose or suggest the formation of a thermal bridge as recited in the claims. In contrast, Applicants have provided an enabling Specification with clear definitions and examples, supported by those skilled in the art, that a thermal bridge formed by biopharmaceutical material does exist by practicing the method and apparatus recited in the claims.

IV. Prior Art Status of the 1996 DMT Article and the 1996 article in Advanstar and the Drug Manufacturing Technology Series, Vol. 2

Applicants admit that the 1996 DMT Article and the 1996 article in Advanstar and the Drug Manufacturing Technology Series, Vol. 2 are prior art to the above-captioned application.

V. Rejection Under 35 U.S.C. §102(b) or §103(a)

Claims 88 and 89 also stand rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over the 1992 publication by Wisniewski and Wu. Applicants respectfully and most strenuously traverse these rejections and reiterate the arguments set forth in the Amendment and Response filed January 7, 2002 and Supplemental Response on January 24, 2002.

With respect to an obviousness rejection, Applicants submit that a valid obviousness rejection requires that the prior art

references, when combined, teach or suggest all of the claimed elements. The Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness.

In the instant application, the Examiner has failed to overcome this burden. Specifically, the Examiner has failed to point to a reference, or combination of references, that teaches or suggests a thermal bridge, as properly defined, formed by a medium comprising a biopharmaceutical product between one or more heat transfer members and the interior wall of a vessel wherein heat is transferred from the heat transfer member through the thermal bridge to the heat transfer member of the interior wall when the interior wall is actively cooled as recited in the claims. As clearly set forth in the Specification, a thermal bridge has a downward temperature gradient from the heat transfer members to the interior wall. As clearly set forth in the Declaration of Mr. Wisniewski, the temperature profile of the 1992 Genentech device includes a higher temperature at a location between the fins and the interior wall, not a downward temperature gradient as required by the definition of a thermal bridge. The Examiner has offered no credible proof that contradicts this assessment of the 1992 Genentech device.

In the Office Action dated July 12, 2002 on page 12, the Examiner incorrectly equates a "thermal bridge" as recited in the claims and taught in the specification with an "ice bridge." Applicants respectfully traverses this comparison. A "thermal bridge" as claimed requires heat to be transferred therethrough in a particular way, e.g. from the heat transfer member to the interior wall - forming a downward temperature gradient from the heat transfer member to the interior wall (e.g. as depicted in Fig. 3(b) of the present application). Applicants do not

dispute the fact that, over time, the Genentech container will form an ice bridge between the fins and the interior wall. However, this ice bridge will not form a downward temperature gradient from the fins to the interior wall.

Instead, a location between the fins and the interior wall of the 1992 Genentech container will have a higher temperature than the fin and the interior wall, even if the medium in the gap is frozen. Heat is transferred from the medium at a location in the gap to the interior wall and to the heat transfer member. In other words, heat is being extracted from a location in the gap between the heat exchange member and the interior wall, not from the heat transfer member to the interior wall as required when a thermal bridge is formed. Thus, as compared to, for example, the downward temperature gradient from the heat transfer member to the interior wall shown in the temperature profile in Fig. 3(b), a temperature profile of the device disclosed in the Wisniewski and Wu publication would show the temperature gradually increasing after the fin to a location in the gap between the fin and the interior wall and then gradually decreasing towards the interior wall. There is absolutely no disclosure or suggestion that such a thermal bridge is formed in the 1992 Genentech container or any other prior art reference on record.

Moreover, the 1992 Wisniewski and Wu teaches away from extending the fins towards the interior wall. Specifically, the publication teaches that the heat transfer fins "were configured to divide the tank volume into compartments to decrease freezing and thawing time and to reduce cryoconcentration effects." See pg. 136, col. 1. Thus, the 1992 Wisniewski and Wu publication already teaches that the fins aid in forming compartments and there is no need to extend the fins towards the walls. There is

simply no suggestion or motivation therefore to extend the fins of the device disclosed by the 1992 Wisniewski and Wu publication towards the interior wall.

Further, none of the references recognizes the advantages of a thermal bridge and/or the problems or disadvantages of freezing without the formation of a thermal bridge. Because the references do not recognize the advantage of forming a thermal bridge, there is simply no motivation or suggestion to one of ordinary skill in the art to arrive at the claimed invention.

The combination of Kaufman, Longardner, and Richelli with the Wisniewski and Wu publication fails to cure this deficiency. Specifically, Kaufman, Longardner and Richelli fail to disclose or suggest, at least, a medium comprising a biopharmaceutical product or a thermal transfer bridge formed by the medium between the one or more heat transfer members and the interior wall wherein heat is transferred from the heat transfer member through the thermal bridge to the interior wall when the interior wall is actively cooled as recited in the claims.

Accordingly, Applicants respectfully submit that the terms "thermal bridge" and "biopharmaceutical product" are definite and that the claims are patentable over the cited references. Because none of the prior art references on record disclose or suggest the formation of a thermal bridge, the Examiner cannot satisfy or overcome his burden of establishing a *prima facie* conclusion of obviousness. Since the Examiner cannot produce a *prima facie* case of non-obviousness, Applicants are under no obligation to submit evidence of non-obviousness. See MPEP §2142.

For these reasons, it is believed that all of the claims as presently presented, are patentable, and that this application

is in allowable condition. Accordingly, allowance of the claims 69-107 is respectfully requested.

Respectfully submitted,



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